510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE

A. 510(k) Number:

K061536

B. Purpose for Submission:

To add *Proteus mirabilis* to the Dried Gram-Negative MIC/Combo Panels for screening and confirmatory testing for extended spectrum Beta- lactamase (ESBL)

C. Measurand:

ESBL screen with: Cefpodoxime (0.015-64 ug/mL), Ceftazidime (0.5-128 µg/mL), and Cefotaxime (0.5-128 µg/mL)

ESBL confirmation with: Ceftazidime (0.5-128 µg/mL), Ceftazidime/clavulanic acid (0.12/4 – 32/4 µg/mL), and Cefotaxime (0.5-128 µg/mL), Cefotaxime/clavulanic acid (0.12/4 -32/4 µg/mL)

D. Type of Test:

Quantitative and Qualitative growth based detection

E. Applicant:

Dade Behring
Dade MicroScan Inc.

F. Proprietary and Established Names:

MicroScan® Dried Gram-Negative MIC/Combo Panels

G. Regulatory Information:

1. Regulation section:
   866.1640 Antimicrobial Susceptibility Test Powder

2. Classification:
   Class II

3. Product code:
   JWY - Manual Antimicrobial Susceptibility Test Systems

LRG-Instrument for Auto Reader & Interpretation of Overnight Antimicrobial Susceptibility Systems
LTT – Panels, Test, Susceptibility, Antimicrobial

4. Panel:
83 Microbiology

H. Intended Use:

1. Intended use(s):

ESBL screen with Cefpodoxime (0.015-64 ug/mL), Ceftazidime (0.5-128 µg/mL), and Cefotaxime (0.5-128 µg/mL) for use with the MicroScan® Dried Gram Negative MIC/Combo Panels and Dreid Gram Negative Breakpoint Combo Panels. MicroScan® panels are designed for use in determining antimicrobial agent susceptibility and/or identification to the species level of aerobic and facultatively anaerobic gram-negative bacilli.

ESBL confirmation with Ceftazidime (0.5-128 µg/mL), Ceftazidime/clavulanic acid (0.12/4 – 32/4 µg/mL), and Cefotaxime (0.5-128 µg/mL), Cefotaxime/clavulanic acid (0.12/4 -32/4 µg/mL) for use with MicroScan® Dried extended-spectrum beta-lactamase (ESBLs) Confirmation Panel. The MicroScan® ESβL *plus* Dried ESBL Confirmation Panel is designed for use in the determination of antimicrobial agent susceptibility of colonies grown on solid media of rapidly-growing gram-negative bacilli and for the detection of ESBL production in *Escherichia coli, Klebsiella oxytoca, Klebsiella pneumonia,* and *Proteus mirabilis.*

2. Indication(s) for use:

To be used in the screening of *Escherichia coli, Klebsiella oxytoca, K. pneumonia,* and *Proteus mirabilis* when testing on the Dried Gram Negative MIC Panels and for the confirmation of Extended-Spectrum Beta – Lactamase production of *Escherichia coli, Klebsiella oxytoca, K. pneumonia,* and *Proteus mirabilis.*

3. Special conditions for use statement(s):
The Prompt® method of inoculation is an alternate method of inoculation preparation that is supported in the methodology along with the turbidity method. The stationary and log inoculum methods should not be used with this antibiotic.

4. Special instrument requirements:

Readings may be performed on the autoSCAN®-4 and WalkAway® Systems.

I. Device Description:

The MicroScan® Dried Gram-Negative MIC/Combo Panel contains microdilutions of each antimicrobial agent in various concentrations with Mueller Hinton Broth and various nutrients which are dehydrated and dried in panels. Each panel contains two control wells: a no-growth control well (contains water only/no nutrients or broth), and a growth control well (contains test medium without antibiotic). The panel is rehydrated and inoculated at the same time with 0.1 ml of suspension prepared by the turbidity method (inoculum prepared in water, then 0.1ml transferred to 25ml of inoculum water containing pluronic-D/F-a wetting solution) for a final inoculum of 3-7 X 10^5. The Prompt® method of inoculation is also recommended as an alternate means of preparing the inoculum. The panels are incubated at 35° C in a non-CO_2 incubator for 16-20 hours and read by visual observation of growth. Panels may be read manually, with the autoSCAN®-4 or WalkAway® Systems.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   MicroScan Dried Gram-Negative MIC/Combo Panels

2. Predicate 510(k) number(s):

   K013423 – ESBL Screen

   K020037 ESBL confirmation

3. Comparison with predicate:

Similarities		
Item	**Device**	**Predicate**
Intended Use	MicroScan® Dried Gram-Negative MIC panels for screening and confirmation of ESBL	Same
Inoculum preparation	Inoculum prepared from isolated colonies using either the Turbidity method or Prompt® system	Same
Technology	Growth based after 16 hours incubation	Same
Results	Report results as screen positive for suspected of harboring an ESBL. Confirmed ESBL producers report as resistant for all penicillins, cephalosporins and aztreonam	Same
Differences		
Item	**Device**	**Predicate**
Test organism	*Proteus mirabilis*	*Escherichia coli, Klebsiella pneumonia, and K. oxytoca*
Antibiotic	ESBL screen with: Cefpodoxime (0.015-64 ug/mL), Ceftazidime (0.5-128 µg/mL), and Cefotaxime (0.5-	Screen includes Ceftazidime, aztreonam, Cefpodoxime, cefotaxime

	128 µg/mL) ESBL confirmation with: Ceftazidime (0.5-128 µg/mL), Ceftazidime/clavulanic acid (0.12/4 – 32/4 µg/mL), and Cefotaxime (0.5-128 µg/mL), Cefotaxime/clavulanic acid (0.12/4 - 32/4 µg/mL)	or ceftriaxone

K. Standard/Guidance Document Referenced (if applicable):

Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems; Guidance for Industry and FDA"; CLSI M7 (M100-S16) "Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard".

L. Test Principle:

After incubation in a non-CO_2 incubator for 16-20 hours, the minimum inhibitory concentration (MIC) for the test organisms are read by determining the lowest antimicrobial concentration showing inhibition of growth. The panels can be read manually and with the autoSCAN®-4 by observing growth or no growth or with the use of the WalkAway® instrument, which uses an optics system with growth algorithms to directly measure organism growth.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. *Precision/Reproducibility:*
   Reproducibility was demonstrated using 6 *P. mirabilis* isolates tested at 3 sites on 3 separate days in triplicate. The study included the testing of both the turbidity inoculum method and Prompt® method of inoculation with readings performed manually, with the autoSCAN®-4 and WalkAway® Systems. All methods provided acceptable reproducibility for the screening and confirmations methods.

   b. *Linearity/assay reportable range:*

   Not Applicable

   c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
   Quality Control with *E. coli* ATCC 25922 and *K. pneumoniae* ATCC 700603 were tested with the expected result on most days using the Prompt® and the turbidity method of inoculation with reading performed manually, with the

autoSCAN®-4 and WalkAway® Systems. The Prompt® failed Quality control on slightly more occasions than the turbidity method of inoculation with the results being out of range on the resistant side of the expected result. The method of reading made no difference in the results.

Inoculum density control: A turbidity meter was used for the turbidity inoculation method with daily checks. The Prompt® method of inoculation had colony counts performed periodically throughout the study to determine the average inoculum density since there is no visual check of the inoculum using this device. The average of the Quality Control recommended isolates were acceptable except for one site that had an occasional colony count with the Prompt® outside the recommended range (on the higher CFU side) for the CLSI reference method.

d. Detection limit:

Not Applicable

e. Analytical specificity:

Not Applicable

f. Assay cut-off:

Not Applicable

2. Comparison studies:

a. Method comparison with predicate device:
Clinical testing was performed at three sites with fresh isolates of *Proteus mirabilis* supplemented with stock isolates and inoculated using the turbidity inoculation method. A comparison of the MicroScan® Dried Gram-Negative test panel results was made to the results from the reference broth method conducted as recommended in the CLSI standard M7-A6 with the following deviations from that recommendation**;** Pluronic-F is used as the inoculum in the frozen reference panels. This is composed of water which contains a very small amount (0.1) of Pluronic P104 to provide a smoother draw of liquid into the inoculator. An internal validation study was performed that demonstrated there was no difference with these antibiotics and *P. mirabilis* when this wetting solution was used.

Of the 81 clinical isolates tested, 68 were ESBL negative of which two were ESBL screen positive but did not confirm using the ESBL confirmatory test. There were 13 positive results for ESBL by the reference method and these were all screen positive and confirmed as ESBL positive using the MicroScan® confirmatory testing for ESBL.

A challenge set consisting of 35 *P. mirabilis* that were previously molecular characterized were tested at one site. Thirteen of these were ESBL positive. These 35 were tested with both the Prompt® and the turbidity methods of inoculation. Readings were performed manually and with both automated methods with acceptable results.

b. Matrix comparison:

Not Applicable

3. Clinical studies:

a. Clinical Sensitivity:

Not Applicable

b. Clinical specificity:

Not Applicable

c. Other clinical supportive data (when a. and b. are not applicable):

Not Applicable

4. Clinical cut-off:

Not Applicable

5. Expected values/Reference range:
The prevalence of ESBL confirmed positive *Proteus mirabilis* is very low at this time.

N. Proposed Labeling:

Quality Control testing is the same as recommended in the reference method described by CLSI and is included in the package insert.

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.